Amendments to the Specification:

At page 1, please replace the title with the following title:

~~**Compositions, Splice Variants and Methods**~~ **Isolated Nucleic Acids Relating to Cancer** ~~**Specific Genes and Proteins**~~

Please replace the paragraph beginning at page 1, line 21 with the following:

Breast cancer, also referred to as mammary tumor cancer, is the second most common cancer among women, accounting for a third of the cancers diagnosed in the United States. One in nine women will develop breast cancer in her lifetime and about 192,000 new cases of breast cancer are diagnosed annually with about 42,000 deaths. Bevers, *Primary Prevention of Breast Cancer*, in Breast Cancer, 20-54 (Kelly K Hunt et al., ed., 2001); Kochanek *et al.*, 49 *Nat'l.Vital Statistics Reports* 1, 14 (2001). Breast cancer is extremely rare in women younger than 20 and is very rare in women under 30. The incidence of breast cancer rises with age and becomes significant by age 50. White Non-Hispanic women have the highest incidence rate for breast cancer and Korean women have the lowest. Increased prevalence of the genetic mutations BRCA1 and BRCA2 that promote breast and other cancers are found in Ashkenazi Jews. African American women have the highest mortality rate for breast cancer among these same groups (31 per 100,000), while Chinese women have the lowest at 11 per 100,000. Although men can get breast cancer, this is extremely rare. In the United States it is estimated there will be 217,440 new cases of breast cancer and 40,580 deaths due to breast cancer in 2004.

(American Cancer Society Website: ~~http://www.cancer.org~~ cancer with the extension .org of the world wide web). With the exception of those cases with associated genetic factors, precise causes of breast cancer are not known.

Please replace the paragraph beginning at page 6, line 8 with the following:

Cancer of the ovaries is the fourth-most common cause of cancer death in women in the United States, with more than 23,000 new cases and roughly 14,000 deaths predicted for the year 2001. Shridhar, V. et al., *Cancer Res.* 61(15): 5895-904 (2001); Memarzadeh, S. & Berek, J. S., *J. Reprod. Med.* 46(7): 621-29 (2001). The American Cancer Society estimates that there will be about 25,580 new cases of ovarian cancer in 2004 in the United States alone. Ovarian cancer will cause about 16,090 deaths in the United States. ACS Website: ~~http://www.cancer.org~~ cancer with the extension .org of the world wide web. The incidence of ovarian cancer is of serious concern worldwide, with an estimated 191,000 new cases predicted annually. Runnebaum, I. B. & Stickeler, E., *J. Cancer Res. Clin. Oncol.* 127(2): 73-79 (2001). Unfortunately, women with ovarian cancer are typically asymptomatic until the disease has metastasized. Because effective screening for ovarian cancer is not available, roughly 70% of women diagnosed have an advanced stage of the cancer with a five-year survival rate of ~25-30%. Memarzadeh, S. & Berek, J. S., *supra;* Nunns, D. et al., *Obstet. Gynecol. Surv.* 55(12): 746-51. Conversely, women diagnosed with early stage ovarian cancer enjoy considerably higher survival rates. Werness, B. A. & Eltabbakh, G. H., *Int'l. J. Gynecol. Pathol.* 20(1): 48-63 (2001). Although our understanding

of the etiology of ovarian cancer is incomplete, the results of extensive research in this area point to a combination of age, genetics, reproductive, and dietary/environmental factors. Age is a key risk factor in the development of ovarian cancer: while the risk for developing ovarian cancer before the age of 30 is slim, the incidence of ovarian cancer rises linearly between ages 30 to 50, increasing at a slower rate thereafter, with the highest incidence being among septagenarian women. Jeanne M. Schilder et al., *Heriditary Ovarian Cancer: Clinical Syndromes and Management*, in Ovarian Cancer 182 (Stephen C. Rubin & Gregory P. Sutton eds., 2d ed. 2001).

Please replace the paragraph beginning at page 11, line 1 with the following:

Colorectal cancer is the second most common cause of cancer death in the United States and the third most prevalent cancer in both men and women. M. L. Davila & A. D. Davila, *Screening for Colon and Rectal Cancer, in* Colon and Rectal Cancer 47 (Peter S. Edelstein ed., 2000). The American Cancer Society estimates that there will be about 106,370 new cases of colon cancer and 40,570 new cases of rectal cancer in the 2004 in the United States alone. Colon cancer and rectal cancer will cause about 56,730 deaths combined in the United States. ACS Website: ~~http://www.cancer.org~~ cancer with the extension .org of the world wide web. Nearly all cases of colorectal cancer arise from adenomatous polyps, some of which mature into large polyps, undergo abnormal growth and development, and ultimately progress into cancer. Davila at 55-56. This progression would appear to

take at least 10 years in most patients, rendering it a readily treatable form of cancer if diagnosed early, when the cancer is localized. Davila at 56; Walter J. Burdette, Cancer: Etiology, Diagnosis, and Treatment 125 (1998).

Please replace the paragraph beginning at page 18, line 1 with the following:

Throughout the last hundred years, the incidence of lung cancer has steadily increased, so much so that now in many countries, it is the most common cancer. In fact, lung cancer is the second most prevalent type of cancer for both men and women in the United States and is the most common cause of cancer death in both sexes. Lung cancer deaths have increased ten-fold in both men and women since 1930, primarily due to an increase in cigarette smoking, but also due to an increased exposure to arsenic, asbestos, chromates, chloromethyl ethers, nickel, polycyclic aromatic hydrocarbons and other agents. *See* Scott, Lung Cancer: A Guide to Diagnosis and Treatment, Addicus Books (2000) and Alberg *et al.*, in Kane *et al.* (eds.) Biology of Lung Cancer, pp. 11-52, Marcel Dekker, Inc. (1998). The American Cancer Society estimates there will be over 173,000 new cases of lung cancer in 2004. Additionally, there will be an estimated 160,440 deaths from lung cancer in 2004. ACS Website: ~~http://www.cancer.org~~ cancer with the extension .org of the world wide web.

Please replace the paragraph beginning at page 24, line 5 with the following:

Recently, the National Comprehensive Cancer Network (NCCN; ~~www.nccn.org~~ nccn with the extension .org of the world wide web), an alliance of nineteen of the world's leading cancer centers,

announces a major update of the NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines. The NCCN is widely recognized as a standard for clinical policy in oncology.

Please replace the paragraph beginning at page 24, line 16 with the following:

Chemotherapeutic agents are specified as two-agent regimens for first-line therapy, two agent regimens or single agents for second-line therapy, and one single agent for third-line therapy. Agents used in first- and second-line therapy are: cisplatin (~~Platinol®~~ PLATINOL, Bristol-Myers Squibb Company), carboplatin (~~Paraplatin®~~ PARAPLATIN, Bristol-Myers Squibb Company), paclitaxel (~~Taxol®~~ TAXOL, Bristol-Myers Squibb Company), docetaxel (~~Taxotere®~~ TAXOTERE, Aventis Pharmaceuticals Inc.), vinorelbine (~~Navelbine®~~ NAVELBINE, GlaxoSmithKline), gemcitabine (~~Gemzar®~~ GEMZAR, Eli Lilly and Company), etoposide (~~Toposar®~~ TOPOSAR, Pfizer, Inc.; ~~VePesid®~~ VEPESID, Bristol-Myers Squibb Company; ~~Etopophos®~~ ETOPOPHOS, Bristol-Myers Squibb Company), irinotecan (~~Camptosar®~~ CAMPTOSAR, Pfizer, Inc.), vinblastine (~~Velban®~~ VELBAN, Eli Lilly and Company), mitomycin (~~Mutamycin®~~ MUTAMYCIN, Bristol-Myers Squibb Company), and ifosfamide (~~Ifex®~~ IFEX, Bristol-Myers Squibb Company).

Please replace the paragraph beginning at page 26, line 1 with the following:

Prostate cancer is the most prevalent cancer in men and is the second leading cause of death from cancer among males in the United States. AJCC Cancer Staging Handbook 203 (Irvin D. Fleming et al. eds., 5th ed. 1998); Walter J. Burdette, Cancer: Etiology, Diagnosis, and Treatment 147 (1998). In 1999, it was estimated that 37,000 men in the United States would die as result of

prostate cancer. Elizabeth A. Platz et al., & Edward Giovannucci, *Epidemiology of and Risk Factors for Prostate Cancer, in* Management of Prostate Cancer 21 (Eric A Klein, ed. 2000). More recently, the American Cancer Society estimated there will be 230,110 new cases of prostate cancer and 29,900 deaths in 2004. American Cancer Society website: ~~www.cancer.org~~ cancer with the extension .org of the world wide web. Cancer of the prostate typically occurs in older males, with a median age of 74 years for clinical diagnosis. Burdette, *supra* at 147. A man's risk of being diagnosed with invasive prostate cancer in his lifetime is one in six. Platz et al., *supra* at 21.

Please replace the paragraph beginning at page 35, line 10 with the following:

FIGURE 1A through 1I displays an alignment of the DNA sequences for DEX0477_016.nt.1 (Pcan057;SEQ ID NO:28) and DEX0477_016.nt.2 (Pcan057v1;SEQ ID NO:29);

Please replace the paragraph beginning at page 35, line 12 with the following:

FIGURE 2A through 2C displays an alignment of the protein sequences for DEX0477_016.aa.1 (Pcan057.aa; SEQ ID NO:180) and DEX0477_016.aa.3 (Pcan057v1.aa; SEQ ID NO:182);

Please replace the paragraph beginning at page 35, line 14 with the following:

FIGURE 3A through 3F displays an alignment of the DNA sequences for DEX0477_001.nt.1 (Pro108; SEQ ID NO:1) and DEX0477_001.nt.2 (Pro177; SEQ ID NO:2);

Please replace the paragraph beginning at page 35, line 16 with the following:

FIGURE 4 displays and alignment of the protein sequences for DEX0477_001.aa.1 (Pro108.aa; SEQ ID NO:142) and DEX0477_001.aa.3 (Pro177.aa; SEQ ID NO:144);

Please replace the paragraph beginning at page 35, line 18 with the following:

FIGURE 5A through 5B displays an alignment of the protein sequences for DEX0477_001.aa.1 (Pro108.aa; SEQ ID NO:142) and DEX0477_001.aa.2 (Pro177.orf; SEQ ID NO:143).

Please replace the paragraph beginning at page 69, line 1 with the following:

Numerous methods exist for detecting SNPs within a nucleotide sequence. A review of many of these methods can be found in Landegren *et al.*, 8 *Genome Res.* 769-76 (1998). For example, a SNP in a genomic sample can be detected by preparing a Reduced Complexity Genome (RCG) from the genomic sample, then analyzing the RCG for the presence or absence of a SNP. See, e.g., WO 00/18960. Multiple SNPs in a population of target polynucleotides in parallel can be detected using, for example, the methods of WO 00/50869. Other SNP detection methods include the methods of U.S. Pat. Nos. 6,297,018 and 6,322,980. Furthermore, SNPs can be detected by restriction fragment length polymorphism (RFLP) analysis. See, e.g., U.S. Pat. Nos. 5,324,631; 5,645,995. RFLP analysis of SNPs, however, is limited to cases where the SNP either creates or destroys a restriction enzyme cleavage site. SNPs can also be detected by direct sequencing of the nucleotide sequence of interest. In addition, numerous assays based on hybridization have

also been developed to detect SNPs and mismatch distinction by polymerases and ligases. Several web sites provide information about SNPs including Ensembl (~~www.ensembl.org~~ ensembl with the extension .org of the world wide web), Sanger Institute (~~http://www.sanger.ac.uk/genetics/exon/~~sanger with the extension .ac.uk/genetics/exon/ of the world wide web), National Center for Biotechnology Information (NCBI) (~~http://www.ncbi.nlm.nih.gov/SNP/~~ ncbi with the extension .nlm.nih.gov/SNP/ of the world wide web), The SNP Consortium Ltd. (~~http://snp.cshl.org/~~ http://snp with the extension .cshl.org/ of the world wide web). The chromosomal locations for the compositions disclosed herein are provided below. In addition, one of ordinary skill in the art could perform a search against the genome or any of the databases cited above using BLAST to find the chromosomal location or locations of SNPs. Another a preferred method to find the genomic coordinates and associated SNPs would be to use the BLAT tool (genome.ucsc.edu, Kent et al. 2001, The Human Genome Browser at UCSC, Genome Research 996-1006 or Kent 2002 BLAT, The BLAST -Like Alignment Tool Genome ~~Reseach~~ Research, 1-9). All web sites above were accessed December 3, 2003.

Please replace the paragraph beginning at page 95, line 27 with the following:

One may determine whether a polypeptide of the invention is likely to be post-translationally modified by analyzing the sequence of the polypeptide to determine if there are peptide motifs indicative of sites for post-translational modification. There are a number of computer programs that permit prediction of post-translational modifications. See, e.g., ~~www.expasy.org~~ expasy with the extension .org of the world wide web (accessed

November 11, 2002), which includes PSORT, for prediction of protein sorting signals and localization sites, SignalP, for prediction of signal peptide cleavage sites, MITOPROT and Predotar, for prediction of mitochondrial targeting sequences, NetOGlyc, for prediction of type O-glycosylation sites in mammalian proteins, big-PI Predictor and DGPI, for prediction of prenylation-anchor and cleavage sites, and NetPhos, for prediction of Ser, Thr and Tyr phosphorylation sites in eukaryotic proteins. Other computer programs, such as those included in GCG, also may be used to determine post-translational modification peptide motifs.

Please replace the paragraph beginning at page 101, line 2 with the following:

In another embodiment, the invention provides polypeptides that have been post-translationally modified. In one embodiment, polypeptides may be modified enzymatically or chemically, by addition or removal of a post-translational modification. For example, a polypeptide may be glycosylated or deglycosylated enzymatically. Similarly, polypeptides may be phosphorylated using a purified kinase, such as a MAP kinase (e.g, p38, ERK, or JNK) or a tyrosine kinase (e.g., Src or erbB2). A polypeptide may also be modified through synthetic chemistry. Alternatively, one may isolate the polypeptide of interest from a cell or tissue that expresses the polypeptide with the desired post-translational modification. In another embodiment, a nucleic acid molecule encoding the polypeptide of interest is introduced into a host cell that is capable of post-translationally modifying the encoded polypeptide in the desired fashion. If the

polypeptide does not contain a motif for a desired post-translational modification, one may alter the post-translational modification by mutating the nucleic acid sequence of a nucleic acid molecule encoding the polypeptide so that it contains a site for the desired post-translational modification. Amino acid sequences that may be post-translationally modified are known in the art. See, e.g., the programs described above on the website ~~www.expasy.org~~ expasy with the extension .org of the world wide web. The nucleic acid molecule may also be introduced into a host cell that is capable of post-translationally modifying the encoded polypeptide. Similarly, one may delete sites that are post-translationally modified by either mutating the nucleic acid sequence so that the encoded polypeptide does not contain the post-translational modification motif, or by introducing the native nucleic acid molecule into a host cell that is not capable of post-translationally modifying the encoded polypeptide.

Please replace the paragraph beginning at page 250, line 26 with the following:

Alignments between previously identified sequences and splice variant sequences are performed to confirm unique portions of splice variant nucleic acid and amino acid sequences. The alignments are done using the Needle program in the European Molecular Biology Open Software Suite (EMBOSS) version 2.2.0 available at www.emboss.org from EMBnet (~~http://www.embnet.org~~ embnet with the extension .org of the world wide web). Default settings are used unless otherwise noted. The Needle program in EMBOSS implements the Needleman-Wunsch algorithm. Needleman, S. B., Wunsch, C. D., *J. Mol. Biol.* 48:443-453 (1970).

Please replace the paragraph beginning at page 394, line 3 with the following:

The sensitivity for Cln224v1 expression was calculated for the cancer samples versus normal samples. The sensitivity value indicates the percentage of cancer samples that show levels of Cln224v1 at least 2 fold higher than the normal tissue or the corresponding normal adjacent ~~form~~ from the same patient.